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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : M. Amin Arnaout et al. Art Unit : 1645  
Serial No. : 09/805,354 Examiner :  
Filed : March 13, 2001  
Title : HIGH AFFINITY INTEGRIN POLYPEPTIDES AND USES THEREOF

Commissioner for Patents  
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the claims:

Cancel claims 1-12.

Add new claims 13-45.

--13. An isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of:

(a) a CD11b  $\alpha$  subunit polypeptide having the Ile at position 332 replaced with an amino acid selected from the group consisting of Gly and Ala;

(b) a polypeptide comprising amino acids 144 to 332 of CD11b  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala;

(c) a polypeptide consisting of amino acids 144 to 331 of CD11b  $\alpha$  subunit;

(d) a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Phe at amino acid 313 and the Ala at amino acid 320 have been replaced by Cys;

(e) a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Val at amino acid 315 and the Ala at amino acid 320 have been replaced by Cys;

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## CERTIFICATE OF MAILING BY FIRST CLASS MAIL

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Carrie A. Amonte

Carrie A. Amonte

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02 FC:203 72.00 OP

(f) a CD11b  $\alpha$  subunit polypeptide having the Ile at position 332 replaced with an amino acid other than Ile; and

(g) a polypeptide comprising amino acids 144 to 332 of CD11b  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid other than Ile.

14. A polypeptide selected from the group consisting of:

(a) a CD11b  $\alpha$  subunit polypeptide having the Ile at position 332 replaced with an amino acid selected from the group consisting of Gly and Ala;

(b) a polypeptide comprising amino acids 144 to 332 of CD11b  $\alpha$  subunit wherein the Ile at position 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala;

(c) a polypeptide comprising amino acids 144 to 331 of CD11b  $\alpha$  subunit, the polypeptide not comprising amino acids 332 to 1152 of CD11b  $\alpha$  subunit;

(d) a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Phe at amino acid 313 and the Ala at amino acid 320 have been replaced by Cys;

(e) a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Val at amino acid 315 and the Ala at amino acid 320 have been replaced by Cys;

(f) a CD11b  $\alpha$  subunit polypeptide having the Ile at position 332 replaced with an amino acid other than Ile; and

(g) a polypeptide comprising amino acids 144 to 332 of CD11b  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid other than Ile.

15. An isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of:

(a) a CD11a  $\alpha$  subunit polypeptide having the Ile at position 331 replaced with an amino acid selected from the group consisting of Gly and Ala;

(b) a polypeptide comprising amino acids 150 to 331 of CD11a  $\alpha$  subunit wherein the Ile at amino acid 331 has been replaced by an amino acid selected from the group consisting of Gly and Ala;

(c) a polypeptide consisting of amino acids 150 to 330 of CD11a  $\alpha$  subunit;

(d) a CD11a  $\alpha$  subunit polypeptide having the Ile at position 331 replaced with an amino acid other than Ile; and

(e) a polypeptide comprising amino acids 150 to 330 of CD11a  $\alpha$  subunit, the polypeptide not comprising amino acids 331 to 1223 of CD11a.

16. A polypeptide selected from the group consisting of:

(a) a CD11a  $\alpha$  subunit polypeptide having the Ile at position 331 replaced with an amino acid selected from the group consisting of Gly and Ala;

(b) a polypeptide comprising amino acids 150 to 331 of CD11a  $\alpha$  subunit wherein the Ile at amino acid 331 has been replaced by an amino acid selected from the group consisting of Gly and Ala;

(c) a polypeptide consisting of amino acids 150 to 330 of CD11a  $\alpha$  subunit;

(d) a CD11a  $\alpha$  subunit polypeptide having the Ile at position 331 replaced with an amino acid other than Ile; and

(e) a polypeptide comprising amino acids 150 to 330 of CD11a  $\alpha$  subunit, the polypeptide not comprising amino acids 331 to 1223 of CD11a.

17. A method for determining whether a test compound is a candidate compound for binding to CD11b, comprising:

(a) contacting a test compound with a polypeptide comprising amino acids 144 to 332 of CD11b  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala, and

(b) determining whether the test compound binds to the polypeptide, wherein a compound which binds to the polypeptide is a candidate compound for binding to CD11b.

18. A method for generating an antibody that selectively binds to a polypeptide comprising the open form of CD11b, the method comprising:

(a) inoculating a non-human mammal with a polypeptide comprising amino acids 144 to 332 of CD11b  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala; and

(b) isolating from the mammal an antibody that selectively binds to a polypeptide comprising the open form of CD11b.

19. An antibody that selectively binds to a polypeptide consisting of acids 144 to 332 of CD11b  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

20. A method for determining whether a test compound is a candidate compound for treating an inflammatory disorder, comprising:

(a) contacting a test compound with a polypeptide comprising amino acids 144 to 332 of CD11b  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala, and

(b) determining whether the test compound binds to the polypeptide,  
wherein a compound which binds to the polypeptide is a candidate compound for treating an inflammatory disorder.

21. A method for determining whether a test compound is a candidate compound for binding to CD11b, comprising:

(a) contacting a test compound with a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Phe at amino acid 313 and the Ala at amino acid 320 have been replaced by Cys, and

(b) determining whether the test compound binds to the polypeptide,  
wherein a compound which binds to the polypeptide is a candidate compound for binding to CD11b.

22. A method for generating an antibody that selectively binds to a polypeptide comprising the open form of CD11b, the method comprising:

(a) inoculating a non-human mammal with a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Phe at amino acid 313 and the Ala at amino acid 320 have been replaced by Cys; and

(b) isolating from the mammal an antibody that selectively binds to a polypeptide comprising the open form of CD11b.

23. An antibody that selectively binds to a polypeptide consisting of amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Phe at amino acid 313 and the Ala at amino acid 320 have been replaced by Cys.

24. A method for determining whether a test compound is a candidate compound for treating an inflammatory disorder, comprising:

(a) contacting a test compound with a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Phe at amino acid 313 and the Ala at amino acid 320 have been replaced by Cys, and

(b) determining whether the test compound binds to the polypeptide,  
wherein a compound which binds to the polypeptide is a candidate compound for treating an inflammatory disorder.

25. A method for determining whether a test compound is a candidate compound for binding to CD11b, comprising:

(a) contacting a test compound with a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Val at amino acid 315 and the Ala at amino acid 320 have been replaced by Cys, and

(b) determining whether the test compound binds to the polypeptide,  
wherein a compound which binds to the polypeptide is a candidate compound for binding to CD11b.

26. A method for generating an antibody that selectively binds to a polypeptide comprising the open form of CD11b, the method comprising:

(a) inoculating a non-human mammal with a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Val at amino acid 315 and the Ala at amino acid 320 have been replaced by Cys; and

(b) isolating from the mammal an antibody that selectively binds to a polypeptide comprising the open form of CD11b.

27. An antibody that selectively binds to a polypeptide consisting of amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Val at amino acid 315 and the Ala at amino acid 320 have been replaced by Cys.

28. A method for determining whether a test compound is a candidate compound for treating an inflammatory disorder, comprising:

(a) contacting a test compound with a polypeptide comprising amino acids 144 to 320 of CD11b  $\alpha$  subunit wherein the Val at amino acid 315 and the Ala at amino acid 320 have been replaced by Cys, and

(b) determining whether the test compound binds to the polypeptide,  
wherein a compound which binds to the polypeptide is a candidate compound for treating an inflammatory disorder.

29. An isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of:

(a) a polypeptide comprising amino acids 144 to 332 of CD11c  $\alpha$  subunit wherein the Ile at position 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala;

(b) a CD11c  $\alpha$  subunit polypeptide having the Ile at position 333 replaced with an amino acid other than Ile;

(c) a polypeptide consisting of amino acids 144 to 332 of CD11c  $\alpha$  subunit;

(d) a polypeptide comprising amino acids 144 to 333 of CD11c  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid other than Ile; and

(e) a CD11c  $\alpha$  subunit polypeptide having the Ile at position 333 replaced with an amino acid other than Ile.

30. A polypeptide selected from the group consisting of:

(a) a polypeptide comprising amino acids 144 to 332 of CD11c  $\alpha$  subunit wherein the Ile at position 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala;

(b) a CD11c  $\alpha$  subunit polypeptide having the Ile at position 333 replaced with an amino acid other than Ile;

(c) a polypeptide consisting of amino acids 144 to 332 of CD11c  $\alpha$  subunit;

(d) a polypeptide comprising amino acids 144 to 333 of CD11c  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid other than Ile; and

(e) a CD11c  $\alpha$  subunit polypeptide having the Ile at position 333 replaced with an amino acid other than Ile.

31. An isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of:

(a) a CD11d  $\alpha$  subunit polypeptide having the Ile at position 332 replaced with an amino acid other than Ile;

(b) a polypeptide consisting of amino acids 144 to 331 of CD11d  $\alpha$  subunit;

(c) a polypeptide comprising amino acids 144 to 332 of CD11d  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid other than Ile;

(d) a CD11d  $\alpha$  subunit polypeptide having the Ile at position 332 replaced with an amino acid selected from the group consisting of Gly and Ala; and

(e) a polypeptide comprising amino acids 144 to 332 of CD11d  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

32. A polypeptide selected from the group consisting of:

(a) a CD11d  $\alpha$  subunit polypeptide having the Ile at position 332 replaced with an amino acid other than Ile;

(b) a polypeptide consisting of amino acids 144 to 331 of CD11d  $\alpha$  subunit;

(c) a polypeptide comprising amino acids 144 to 332 of CD11d  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid other than Ile;

(d) a CD11d  $\alpha$  subunit polypeptide having the Ile at position 332 replaced with an amino acid selected from the group consisting of Gly and Ala; and

(e) a polypeptide comprising amino acids 144 to 332 of CD11d  $\alpha$  subunit wherein the Ile at amino acid 332 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

33. An isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of

(a) a CD49a  $\alpha$  subunit polypeptide having the Ile at position 331 replaced with an amino acid other than Ile;

(b) a polypeptide consisting of amino acids 144 to 330 of CD49a  $\alpha$  subunit;

(c) a polypeptide comprising amino acids 144 to 332 of CD49a  $\alpha$  subunit wherein the Ile at amino acid 331 has been replaced by an amino acid other than Ile;

(d) a CD49a  $\alpha$  subunit polypeptide having the Ile at position 331 replaced with an amino acid other than Ile; and

(e) a polypeptide comprising amino acids 144 to 332 of CD49a  $\alpha$  subunit wherein the Ile at amino acid 331 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

34. A polypeptide selected from the group consisting of:

(a) a CD49a  $\alpha$  subunit polypeptide having the Ile at position 331 replaced with an amino acid other than Ile;

(b) a polypeptide consisting of amino acids 144 to 330 of CD49a  $\alpha$  subunit;

(c) a polypeptide comprising amino acids 144 to 332 of CD49a  $\alpha$  subunit wherein the Ile at amino acid 331 has been replaced by an amino acid other than Ile;



(d) a CD49a  $\alpha$  subunit polypeptide having the Ile at position 331 replaced with an amino acid other than Ile; and

(e) a polypeptide comprising amino acids 144 to 332 of CD49a  $\alpha$  subunit wherein the Ile at amino acid 331 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

35. An isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of:

(a) a CD49b  $\alpha$  subunit polypeptide having the Ile at position 361 replaced with an amino acid other than Ile;

(b) a CD49b  $\alpha$  subunit polypeptide having the Ile at position 361 replaced with an amino acid selected from the group consisting of Gly and Ala;

(c) a polypeptide consisting of amino acids 144 to 360 of CD49b  $\alpha$  subunit;

(d) a polypeptide comprising amino acids 144 to 361 of CD49b  $\alpha$  subunit wherein the Ile at amino acid 361 has been replaced by an amino acid other than Ile; and

(e) a polypeptide comprising amino acids 144 to 361 of CD49b  $\alpha$  subunit wherein the Ile at amino acid 361 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

36. A polypeptide selected from the group consisting of:

(a) a CD49b  $\alpha$  subunit polypeptide having the Ile at position 361 replaced with an amino acid other than Ile;

(b) a CD49b  $\alpha$  subunit polypeptide having the Ile at position 361 replaced with an amino acid selected from the group consisting of Gly and Ala;

(c) a polypeptide consisting of amino acids 144 to 360 of CD49b  $\alpha$  subunit;

(d) a polypeptide comprising amino acids 144 to 361 of CD49b  $\alpha$  subunit wherein the Ile at amino acid 361 has been replaced by an amino acid other than Ile; and

(e) a polypeptide comprising amino acids 144 to 361 of CD49b  $\alpha$  subunit wherein the Ile at amino acid 361 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

37. An isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of:

- (a) an Alpha 10  $\alpha$  subunit polypeptide having the Ile at position 249 replaced with an amino acid other than Ile;
- (b) an Alpha 10  $\alpha$  subunit polypeptide having the Ile at position 249 replaced with an amino acid selected from the group consisting of Gly and Ala;
- (c) a polypeptide consisting of amino acids 57 to 248 of Alpha 10  $\alpha$  subunit;
- (d) a polypeptide comprising amino acids 57 to 249 of Alpha 10  $\alpha$  subunit wherein the Ile at amino acid 249 has been replaced by an amino acid other than Ile; and
- (e) a polypeptide comprising amino acids 57 to 249 of Alpha 10  $\alpha$  subunit wherein the Ile at amino acid 249 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

38. A polypeptide selected from the group consisting of:

- (a) an Alpha 10  $\alpha$  subunit polypeptide having the Ile at position 249 replaced with an amino acid other than Ile;
- (b) an Alpha 10  $\alpha$  subunit polypeptide having the Ile at position 249 replaced with an amino acid selected from the group consisting of Gly and Ala;
- (c) a polypeptide consisting of amino acids 57 to 248 of Alpha 10  $\alpha$  subunit;
- (d) a polypeptide comprising amino acids 57 to 249 of Alpha 10  $\alpha$  subunit wherein the Ile at amino acid 249 has been replaced by an amino acid other than Ile; and
- (e) a polypeptide comprising amino acids 57 to 249 of Alpha 10  $\alpha$  subunit wherein the Ile at amino acid 249 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

39. An isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of:

- (a) an Alpha 11  $\alpha$  subunit polypeptide having the Ile at position 349 replaced with an amino acid other than Ile;

- (b) an Alpha 11  $\alpha$  subunit polypeptide having the Ile at position 349 replaced with an amino acid selected from the group consisting of Gly and Ala;
- (c) a polypeptide consisting of amino acids 159 to 348 of Alpha 11  $\alpha$  subunit;
- (d) a polypeptide comprising amino acids 159 to 349 of Alpha 11  $\alpha$  subunit wherein the Ile at amino acid 349 has been replaced by an amino acid other than Ile; and
- (e) a polypeptide comprising amino acids 159 to 349 of Alpha 11  $\alpha$  subunit wherein the Ile at amino acid 349 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

40. A polypeptide selected from the group consisting of:

- (a) an Alpha 11  $\alpha$  subunit polypeptide having the Ile at position 349 replaced with an amino acid other than Ile;
- (b) an Alpha 11  $\alpha$  subunit polypeptide having the Ile at position 349 replaced with an amino acid selected from the group consisting of Gly and Ala;
- (c) a polypeptide consisting of amino acids 159 to 348 of Alpha 11  $\alpha$  subunit;
- (d) a polypeptide comprising amino acids 159 to 349 of Alpha 11  $\alpha$  subunit wherein the Ile at amino acid 349 has been replaced by an amino acid other than Ile; and
- (e) a polypeptide comprising amino acids 159 to 349 of Alpha 11  $\alpha$  subunit wherein the Ile at amino acid 349 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

41. An isolated nucleic acid molecule encoding a polypeptide selected from the group consisting of:

- (a) an Alpha E  $\alpha$  subunit polypeptide having the Ile at position 385 replaced with an amino acid other than Ile;
- (b) an Alpha E  $\alpha$  subunit polypeptide having the Ile at position 385 replaced with an amino acid selected from the group consisting of Gly and Ala;
- (c) a polypeptide consisting of amino acids 196 to 384 of Alpha 11  $\alpha$  subunit;
- (d) a polypeptide comprising amino acids 196 to 387 of Alpha 11  $\alpha$  subunit wherein the Ile at amino acid 385 has been replaced by an amino acid other than Ile;

(e) a polypeptide comprising amino acids 196 to 387 of Alpha 11  $\alpha$  subunit wherein the Ile at amino acid 385 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

42. A polypeptide selected from the group consisting of:

(a) an Alpha E  $\alpha$  subunit polypeptide having the Ile at position 385 replaced with an amino acid other than Ile;

(b) an Alpha E  $\alpha$  subunit polypeptide having the Ile at position 385 replaced with an amino acid selected from the group consisting of Gly and Ala;

(c) a polypeptide consisting of amino acids 196 to 384 of Alpha 11  $\alpha$  subunit;

(d) a polypeptide comprising amino acids 196 to 387 of Alpha 11  $\alpha$  subunit wherein the Ile at amino acid 385 has been replaced by an amino acid other than Ile; and

(e) a polypeptide comprising amino acids 196 to 387 of Alpha 11  $\alpha$  subunit wherein the Ile at amino acid 385 has been replaced by an amino acid selected from the group consisting of Gly and Ala.

43. A method for treating an inflammatory disorder, the method comprising administering the antibody of any of claims 19, 23, and 27.

44. A method for treating ischemia-reperfusion injury, the method comprising administering the antibody of any of claims 19, 23, and 27.

45. A method for treating restinosis, the method comprising administering the antibody of any of claims 19, 23, and 27.--

Applicant : M. Amin Arnaout et al  
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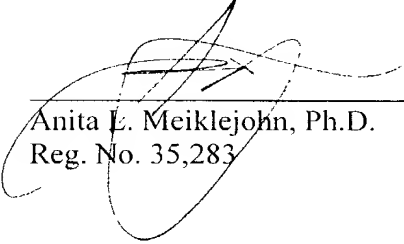
09/805,354, 123101  
Attorney Pocket No.: 00786-536001

Remarks

Applicant asks that all claims be examined. Enclosed is a check in the amount of \$1,085.00 for excess claim fees. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 15 NOV 2001

  
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Anita E. Meiklejohn, Ph.D.  
Reg. No. 35,283

Fish & Richardson P.C.  
225 Franklin Street  
Boston, Massachusetts 02110-2804  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906